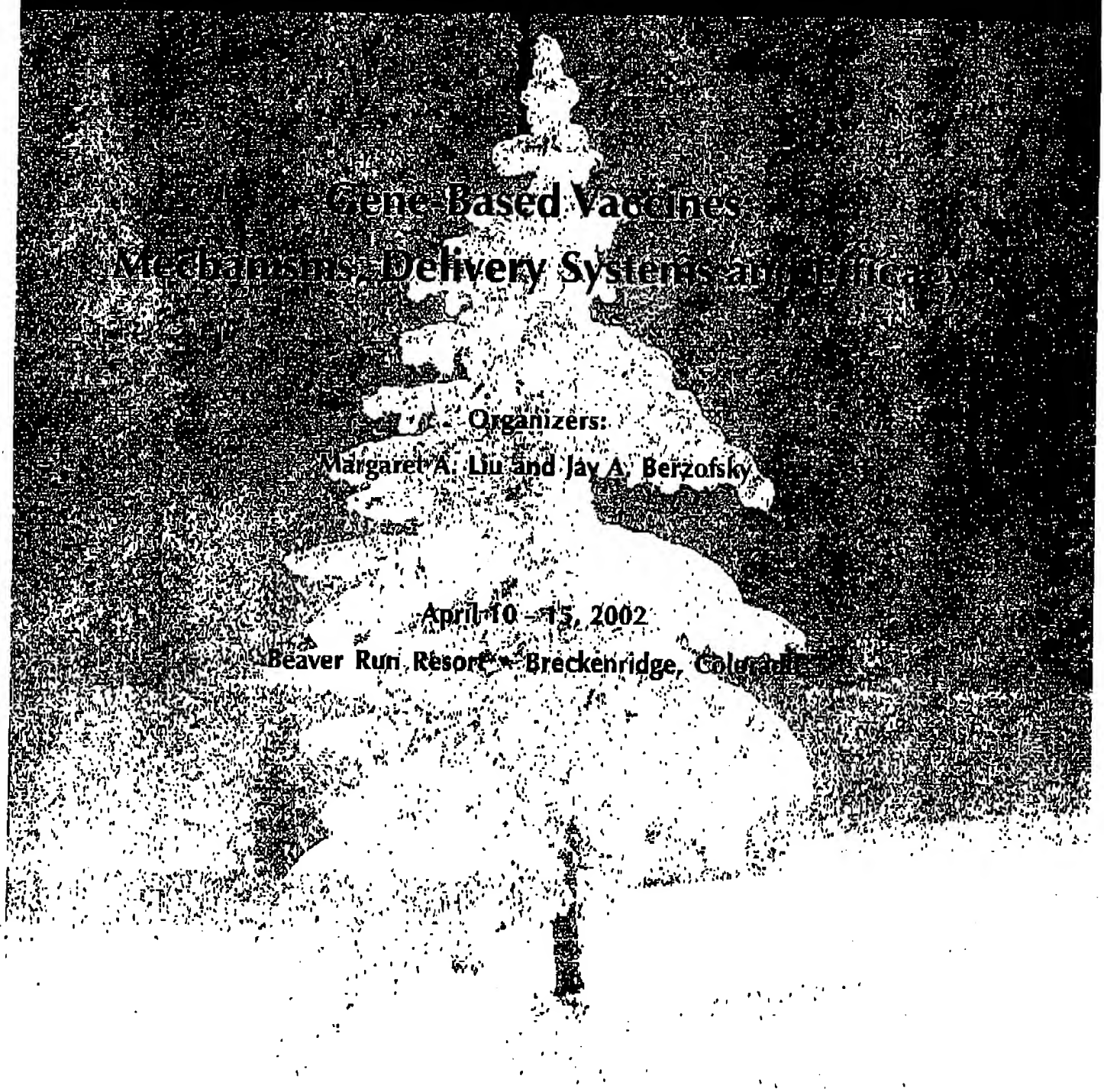
KEYSTONE SYMPOSIA

2002 Abstract Book



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Poster Abstracts

Friday, April 12: Poster Session

205 **A potent alphavirus replicon particle vaccine encoding PSMA for immunotherapy of prostate cancer**

Gardner, J.P., Donovan, G.P., Schülke, N., Morrissey, D.M., Durso, R.J., Cohen, M.A., Arrigale, R.R., Zhan, C., Caley, I and Olson, W.C.*

*The PSMA Development Company LLC, A Joint Venture between Progenics Pharmaceuticals Inc. and Cytogen Corp., Tarrytown, NY 10591, and *AlphaVax, Inc., Research Triangle Park, NC 27709*

The identification and delivery of tumor-specific antigens hold great promise for cancer immunotherapy. Prostate specific membrane antigen (PSMA) is a highly attractive candidate antigen for vaccination because it is abundantly expressed on the surface of prostate cancer cells and on the neovasculature of a wide array of other tumors. Our main goal is to develop PSMA-based immunotherapies with broad utility to optimally train the immune system to recognize and reject neoplastic cells expressing PSMA. We are investigating the potential of a viral-vectored vaccine and a traditional adjuvanted protein immunogen individually and in heterologous prime-boost immunization regimens.

We have selected non-replicating vaccine replicon particles (VRP) based on the alphavirus, Venezuelan equine encephalitis virus, as delivery vehicles because of their efficacy for immunization against infectious disease in several animal models and redundant safety features. VRP infect cells in the draining lymph nodes, where the replicon drives production of large quantities of the heterologous antigen and typically induce robust immune responses.

VRP encoding full-length human PSMA elicited potent, durable Th1-biased cellular and humoral responses in normal BALB/c mice when used as single immunogens. We have now extended this analysis to human HLA-A2 transgenic mice, a more pertinent model for quantification of human Class I-restricted cellular responses, and to heterologous prime-boost vaccination regimens. Mice were immunized with varying doses of VRP alone or combination with recombinant PSMA protein boosts. PSMA-specific immune responses were measured with a panel of cellular and humoral immunoassays, including ELISPOT and intracellular cytokine staining for IFNγ and IL4 in T cell subsets. Our findings demonstrate that encoding PSMA immunogen in the VRP delivery vehicle is a highly promising cancer vaccine strategy and strongly support the advancement of this novel vector system into human clinical testing.